CLAIMS

We claim:

1. A variant RANKL protein, wherein said variant RANKL protein comprises modifications at at least one of the following positions: H180, K181, H189, D190, R191, G192, S197, R223, R223, H225, E226, T227, S228, Q237, K248, I249, H253, S268, E269, F270, R284, S297, D300, and D302.

2. A variant RANKL protein according to claim 1, wherein said substitutions comprise combinations of: a) E269 and F270, b) H225 and E269, c) H225 and F270, d) H225 and E269, e) H225 and F270, f) R191 and I249, g) G192 and H225, h) H225 and I249, I) H225 and I249, j) E226 and I249, k) T227 and K248, l) E226 and I249, m) T227 and K248, n) S228 and I249, o) D190 and K248, p) D190 and H225, q) D190 and K248, r) G192 and H225, s) D190 and H225, t) G192 and K248, u) H225, E226 and F270, v) R191, E226 and K248, w) R191, E226 and K248, x) G192, K248 and F270, y) G192, H225 and I249, and z) G192, H225 and I249.

3. A variant RANKL protein according to claim 1, wherein said variant RANKL protein comprises at least one substation selected from the group consisting of: H180E, K181Q, K181E, H189R, R191Q, R191E, G192A, S197E, R223M, R223E, R223Q, H225T, H225N, H225E, H225R, E226Q, E226D, E226R, T227K, S228E, S228H, Q237T, Q237K, Q237E, K248E, I249Q, H253S, H253T, S268D, E269R, E269T, E269Q, E269K, F270T, F270K, F270E, F270V, R284E, S297Q, D300N, D302H, and D302E.

4. A variant RANKL protein according to claim 1, wherein said substitutions comprise combinations of: a) E269T and F270T, b) H225E and E269K, c) H225E and F270T, d) H225R and E269K, e) H225R and F270T, f) R191E and I249R, g) G192A and H225N, h) H225N and I249R, I) H225R and I249R, j) E226R and I249R, k) T227Q and K248E, l) E226Q and I249R, m) T227K and K248E, n) S228E and I249R, o) D190T and K248E, p) D190T and H225R, q) D190Q and K248E, r) G192A and H225R, s) D190Q and H225R, t) G192A and K248E, u) H225E, E226D and F270T, v) R191K, E226R and K248E, w) R191K, E226Q and K248E, x) G192A, K248E and F270T, y) G192A, H225N and I249R, and z) G192A, H225R and I249R.

5. A variant RANKL protein according to claim 1, wherein said variant RANKL protein comprises at least one substitution selected from the group consisting of: H180E, K181Q, K181E, R191E, R223M, R223E, R223Q, E226R, T227K, S228E, S228H, Q237K, K248E, I249R, E269T, E269Q, D302E, H253S, and H253T.

6. A variant RANKL protein according to claim 1, wherein said variant RANKL protein is an antagonist.

7. A variant RANKL protein according to claim 6, wherein said variant RANKL protein is substantially unable to bind RANK receptor.

8. A variant RANKL protein according to claim 6, wherein said variant RANKL protein is substantially unable to bind OPG.

9. A variant RANKL protein according to claim 6, wherein said variant RANKL protein binds to a RANK receptor but does not substantially activate the RANK receptor.

10. A variant RANKL protein according to claim 9, wherein said variant RANKL protein is substantially unable to bind OPG.

11. A variant RANKL protein according to claim 1, wherein said variant RANKL protein is selected from at least one of the following positions: a) G192, b) R223, c) Q237, d) H225, e) E269, f) I249, g) K248, h) E269 and i) F270.

12. A variant RANKL protein according to claim 11, wherein said substitutions comprise combinations of: (a) H225 and E269; (b) H225 and F270; (c) G192A, H225, and I249); and (d) G192, K248, and F270.

13. A variant RANKL protein according to claim 11, wherein said variant RANKL protein comprises at least one substitution selected from the group consisting of: R223M, R223E, R223Q, and Q237K.

14. A variant RANKL protein according to claim 11, wherein said substitutions comprise combinations of: a) H225R and E269K, b) H225R and F270T, c) G192A, K248E and F270T, d) G192A, H225N and I249R, and e) G192A, H225R and I249R.

15. A variant RANKL protein according to claim 11, wherein said variant RANKL protein does not substantially bind to OPG.

16. A variant RANKL protein according to claim 1, wherein said variant RANKL protein comprises modifications at least one of the following positions: R191, G192, H225, E226, K248, I249, E269, and F270.

17. A variant RANKL protein according to claim 16, wherein said variant RANKL protein comprises at least one pair of substitutions selected from the group consisting of: (a) E269 and F270; (b) H225 and E269; (c) H225 and F270; (d) G192 and H225; (e) H225 and I249; (f) R191, E226 and K248 (g) G192, H225 and I249.

18. A variant RANKL protein according to claim 16, wherein said variant RANKL protein does not substantially bind to RANK.

19. A variant RANKL protein according to claim 16, wherein said variant RANKL protein comprises at least one substitution selected from the group consisting of: H225T, H225N, H225E,

H225R, E226Q, E269R, E269K, F270K, F270E, E269T and F270T, H225E and E269K, H225E and F270T, H225R and E269K, H225R and F270T, G192A and H225N, H225N and I249R, H225R and I249R, G192A and K248E, R191K and E226R and K248E, R191K and E226Q and K248E, G192A and K248E and F270T, and G192A and H225N and I249R.

20. A variant RANKL protein according to claim 1, wherein said variant RANKL protein does not substantially activate osteoclastogenesis.

21. A variant RANKL protein according to claim 20, wherein said variant RANKL protein comprises modifications at at least one of the following positions: K181, D190, R191, G192, R223, H225, E226, T227, S228, Q237, K248, I249, H253, E269, F270, S297, and D302.

22. A variant RANKL protein according to claim 20,wherein said variant RANKL protein comprises modifications at at least one of the following sets of positions: (a) H225 and E269; (b) H225 and F270; (c) R191 and I249; (d) G192 and H225; (e) H225 and I249; (f) T227 and K248; (g) D190 and H225; (h) H225E, E226 and F270; (i) R191, E226, and K248; (j) G192, K248, and F270; and (k) G192, H225 and I249.

23. A variant RANKL protein according to claim 21, wherein said variant RANKL protein comprises at least one substitution selected from the group consisting of: K181Q, K181E, R191Q, R191E, R223M, R223E, H225T, H225N, H225E, H225R, E226Q, E226D, S228E, S228H, Q237K, Q237E, H253S, H253T, E269R, E269T, E269Q, E269K, F270T, F270K, F270E, F270E, S297Q, and D302E.

24. A variant RANKL protein according to claim 21, wherein said variant RANKL protein comprises modifications at at least one of the following sets of positions: a) H225E and E269K, b) H225E and F270T, c) H225R and E269K, d) R191E and I249R, e) G192A and H225N, f) H225N and I249R, g) H225R and I249R, h) 227Q and K248E, i) G192A and H225R, j) D190Q and H225R, k) G192A and K248E, l) H225E, E226D and F270T, m) R191K, E226R and K248E, n) R191K, E226Q and K248E, o) G192A, K248E and F270T, and p) G192A, H225N and I249R.

25. A variant RANKL protein according to claim 1, wherein said variant RANKL protein comprises modifications at at least one of the following positions: in H180, K181, R223, E226, T227, S228, Q237, E269, D302, and H253.

26. A variant RANKL protein according to claim 25, wherein said variant RANKL protein comprises at least one modification selected from the group consisting of: H180E, K181Q, K181E, R223M, R223E, R223Q, E226R, T227K, S228E, S228H, Q237K, E269T, E269Q, 253S, H253T, and D302E.

27. A variant RANKL protein according to claim 1,wherein said variant RANKL protein comprises modifications at at least one of the following sets of positions: a) R191and I249 or b) T227 and K248.

28. A variant RANKL protein according to claim 27, wherein said variant RANKL protein comprises modifications at at least one of the following sets of positions: a) R191E and I249R or b) T227Q and K248E.

29. A variant RANKL protein according to claim 1, wherein said variant RANKL protein functions as a competitive inhibitor of wild type RANKL.

30. A variant RANKL protein according to claim 1, wherein said variant protein is chemically modified.

31. A variant RANKL protein according to claim 28, wherein said chemical modification is selected from the group consisting of: PEGylation; glycosylation; and a fusion of said variant protein to another entity.

32. A pharmaceutical composition comprising a variant RANKL protein according to claim 1 and a pharmaceutical carrier.

33. A method for treating a RANKL-related condition comprising administration of a variant RANKL protein according to claim 1.